EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	64	CDDO	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/11/07 11:34
L2	5	CDDO-Me	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/11/07 11:34
L3	3	l1 and @ad<"20001128"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/11/07 11:37
L4	8	"KONOPLEVA, MARINA".in. or "ANDREEFF, MICHAEL".in. or "SPORN, MICHAEL"".in. "	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/11/07 11:38

09/998,009

11/7/2007

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	JUL 02	LMEDLINE coverage updated
NEWS 3	JUL 02	SCISEARCH enhanced with complete author names
NEWS 4	JUL 02	CHEMCATS accession numbers revised
NEWS 5	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS 6	JUL 16	CAplus enhanced with French and German abstracts
NEWS 7	JUL 18	CA/CAplus patent coverage enhanced
NEWS 8	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 9	JUL 30	USGENE now available on STN
NEWS 10	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 11	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 12	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 13	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 14	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 15	AUG 27	USPATOLD now available on STN
NEWS 16	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 17	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 18	SEP 13	FORIS renamed to SOFIS
NEWS 19	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 20	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 21	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 22	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 23	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 24	OCT 19	BEILSTEIN updated with new compounds

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:41:16 ON 07 NOV 2007

=> file registry

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 11:41:28 ON 07 NOV 2007
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 6 NOV 2007 HIGHEST RN 952567-23-6
DICTIONARY FILE UPDATES: 6 NOV 2007 HIGHEST RN 952567-23-6

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TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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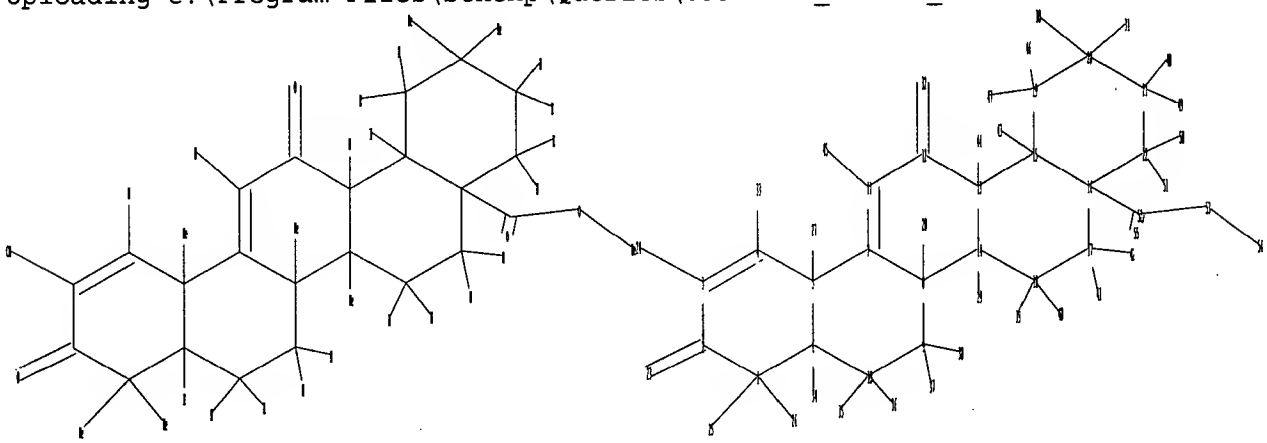
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\09998009_cddome_2.str



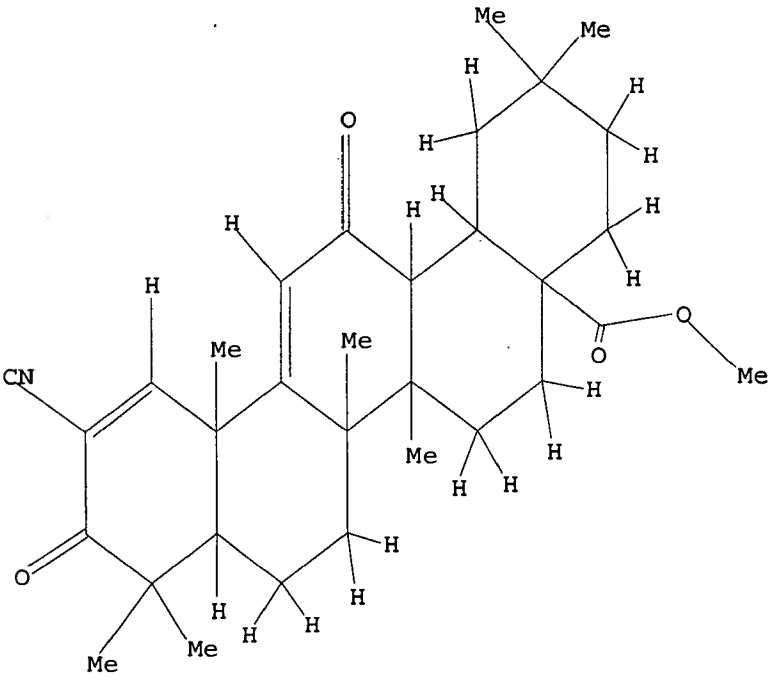
chain nodes :
23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43
44 45 46 47 48 49 50 51 52 53 54 55
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
chain bonds :
1-25 1-26 2-23 3-24 4-33 5-27 6-34 8-28 9-37 9-38 10-35 10-36 11-45
12-32 13-44 14-29 15-43 16-52 17-41 17-42 18-39 18-40 19-46 19-47 20-30
20-31 21-48 21-49 22-50 22-51 52-53 52-55 53-54

ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 7-11 8-9 8-14 9-10 11-12 12-13
13-14 13-15 14-18 15-16 15-19 16-17 16-22 17-18 19-20 20-21 21-22
exact/norm bonds :
1-2 1-6 2-3 2-23 3-4 4-5 5-6 5-7 6-10 7-8 7-11 8-9 8-14 9-10 11-12
12-13 12-32 13-14 13-15 14-18 15-16 15-19 16-17 16-22 17-18 19-20 20-21
21-22 52-53 52-55
exact bonds :
1-25 1-26 3-24 4-33 5-27 6-34 8-28 9-37 9-38 10-35 10-36 11-45 13-44
14-29 15-43 16-52 17-41 17-42 18-39 18-40 19-46 19-47 20-30 20-31 21-48
21-49 22-50 22-51 53-54

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom 22:Atom 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS
28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS
36:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS 43:CLASS
44:CLASS 45:CLASS 46:CLASS 47:CLASS 48:CLASS 49:CLASS 50:CLASS 51:CLASS
52:CLASS 53:CLASS 54:CLASS 55:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 11:41:47 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 7 TO ITERATE

100.0% PROCESSED 7 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 7 TO 298
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 11:41:51 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 113 TO ITERATE

100.0% PROCESSED 113 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

L3 2 SEA SSS FUL L1

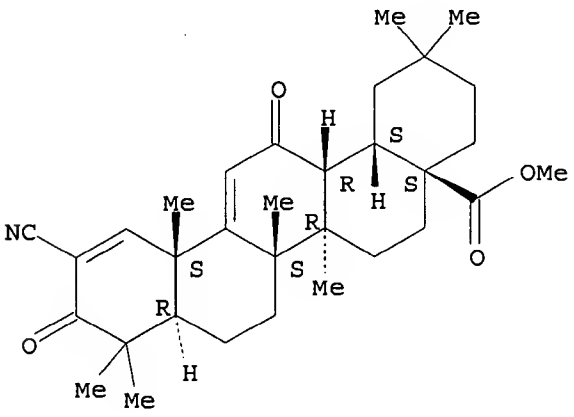
=> d l3

L3 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2007 ACS on STN
RN 418764-26-8 REGISTRY
ED Entered STN: 20 May 2002
CN Oleana-1,9(11)-dien-28-oic acid, 2-cyano-3,12-dioxo-, methyl ester, compd. with methanol (1:1), monohydrate (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H43 N O4 . C H4 O . H2 O
SR CA
LC STN Files: CA, CAPLUS, IMSRESEARCH

CM 1

CRN 218600-53-4
CMF C32 H43 N O4

Absolute stereochemistry. Rotation (+).



CM 2

CRN 67-56-1
CMF C H4 O

H_3C-OH

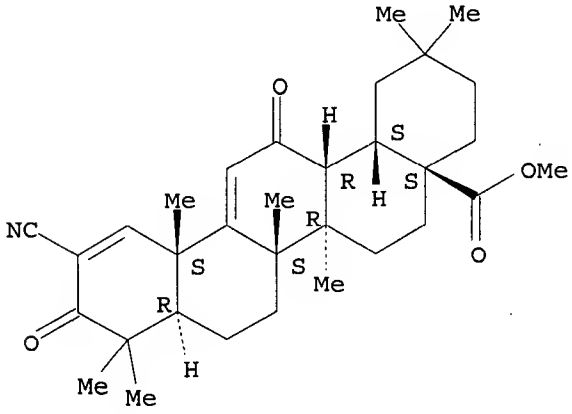
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d scan

L3 2 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN Oleana-1,9(11)-dien-28-oic acid, 2-cyano-3,12-dioxo-, methyl ester
MF C32 H43 N O4
CI COM

Absolute stereochemistry. Rotation (+).



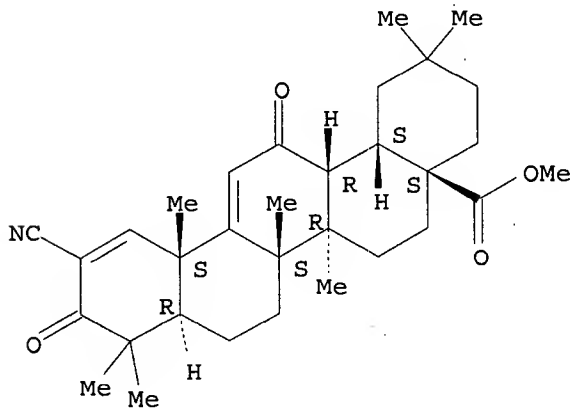
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L3 2 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN Oleana-1,9(11)-dien-28-oic acid, 2-cyano-3,12-dioxo-, methyl ester, compd. with methanol (1:1), monohydrate (9CI)
MF C32 H43 N O4 . C H4 O . H2 O

CM 1

Absolute stereochemistry. Rotation (+).



CM 2

H_3C-OH

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> file medline caplus wpids uspatfull

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	174.50	174.71

FILE 'MEDLINE' ENTERED AT 11:42:29 ON 07 NOV 2007

FILE 'CAPLUS' ENTERED AT 11:42:29 ON 07 NOV 2007
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FILE 'WPIDS' ENTERED AT 11:42:29 ON 07 NOV 2007

FILE 'USPATFULL' ENTERED AT 11:42:29 ON 07 NOV 2007

=> s l3
SAMPLE SEARCH INITIATED 11:42:34 FILE 'WPIDS'
SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:	ONLINE	**COMPLETE**
	BATCH	**COMPLETE**
PROJECTED ITERATIONS:	0 TO	0
PROJECTED ANSWERS:	0 TO	0

L4 30 L3

=> s l4 and (cancer or tumor)
L5 20 L4 AND (CANCER OR TUMOR)

=> d l5 1-20 ibib, abs

L5 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:508813 CAPLUS
DOCUMENT NUMBER: 147:157653
TITLE: The novel triterpenoid C-28 methyleEster of 2-cyano-3, 12-dioxoolen-1, 9-dien-28-oic acid inhibits metastatic murine breast tumor growth through inactivation of STAT3 signaling
AUTHOR(S): Ling, Xiaoyang; Konopleva, Marina; Zeng, Zhihong; Ruvolo, Vivian; Stephens, L. Clifton; Schober, Wendy; McQueen, Teresa; Dietrich, Martin; Madden, Timothy L.; Andreeff, Michael
CORPORATE SOURCE: Section of Molecular Hematology and Therapy, Department of Stem Cell Transplantation and Cellular

Therapy, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Cancer Research (2007), 67(9), 4210-4218
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We and others have reported that C-28 Me ester of 2-cyano-3, 12-dioxoolen-1, 9-dien-28-oic acid (CDDO-Me) effectively inhibits the growth of multiple cancer cell types. Our previous studies indicated that prolonged CDDO-Me treatment inactivated extracellular signal-regulated kinase signaling in acute myelogenous leukemia cells. Whether treatment with CDDO-Me has an earlier effect on other proteins that are important for either signal transduction or oncogenesis is unknown. Constitutively activated signal transducer and activator of transcription 3 (STAT3) is frequently found in human breast cancer samples. Constitutively activated STAT3 was shown to up-regulate c-Myc in several types of cancer and has a feedback effect on Src and Akt. To examine the effects of CDDO-Me on STAT3 signaling in breast cancer, we used the murine 4T1 breast tumor model, which is largely resistant to chemotherapy. In vitro, after treatment of 4T1 cells with 500 nmol/L CDDO-Me for 2 h, we found (a) inactivation of STAT3, (b) inactivation of Src and Akt, (c) 4-fold reduction of c-Myc mRNA levels, (d) accumulation of cells in G2-M cell cycle phase, (e) abrogation of invasive growth of 4T1 cells, and (f) lack of apoptosis induction. In in vivo studies, CDDO-Me completely eliminated 4T1 breast cancer growth and lung metastases induced by 4T1 cells in mice when treatment started 1 day after tumor implantation and significantly inhibited tumor growth when started after 5 days. In vivo studies also indicated that splenic mature dendritic cells were restored after CDDO-Me treatment. In summary, these data suggest that CDDO-Me may have therapeutic potential in breast cancer therapy, in part, through inactivation of STAT3.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:289385 CAPLUS
DOCUMENT NUMBER: 146:492789
TITLE: The Synthetic Triterpenoids CDDO-Methyl Ester and CDDO-Ethyl Amide Prevent Lung Cancer Induced by Vinyl Carbamate in A/J Mice
AUTHOR(S): Liby, Karen; Royce, Darlene B.; Williams, Charlotte R.; Risingsong, Renee; Yore, Mark M.; Honda, Tadashi; Gribble, Gordon W.; Dmitrovsky, Ethan; Sporn, Thomas A.; Sporn, Michael B.
CORPORATE SOURCE: Department of Pharmacology, Dartmouth Med. Sch., Dartmouth Coll., Hanover, NH, USA
SOURCE: Cancer Research (2007), 67(6), 2414-2419
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We report the first use of new synthetic triterpenoids to prevent lung cancer in exptl. animals. Female A/J mice were treated with the mutagenic carcinogen vinyl carbamate, which induces adenocarcinoma of the lung in all animals within 16 wk. If mice were fed either the Me ester or the Et amide derivative of the synthetic triterpenoid 2-cyano-3,12-dioxooleana-1,9(11)-dien-28-oic acid (CDDO-ME and CDDO-EA, resp.), beginning 1 wk after dosing with carcinogen, the number, size, and severity of lung carcinomas were markedly reduced. The mechanisms of action of CDDO-ME and CDDO-EA that are germane to these in vivo findings are the following results shown here in cell culture: (a) suppression of the ability of IFN-γ to induce de novo formation of nitric oxide synthase in a macrophage-like cell line RAW264.7, (b) induction of heme oxygenase-1 in

these RAW cells, and (c) suppression of phosphorylation of the transcription factor signal transducers and activators of transcription 3 as well as induction of apoptosis in human lung cancer cell lines.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1323361 CAPLUS

DOCUMENT NUMBER: 146:308789

TITLE: The synthetic triterpenoid 1-[2-cyano-3,12-dioxooleana-1,9(11)-dien-28-oyl]imidazole blocks nuclear factor-κB activation through direct inhibition of IκB kinase β

AUTHOR(S): Yore, Mark M.; Liby, Karen T.; Honda, Tadashi; Gribble, Gordon W.; Sporn, Michael B.

CORPORATE SOURCE: Department of Pharmacology, Dartmouth Medical School and Department of Chemistry, Dartmouth College, Hanover, NH, USA

SOURCE: Molecular Cancer Therapeutics (2006), 5(12), 3232-3239
CODEN: MCTOCF; ISSN: 1535-7163

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The synthetic triterpenoid 1-[2-cyano-3,12-dioxooleana-1,9(11)-dien-28-oyl]imidazole (CDDO-Im) is a multifunctional agent with potent anti-inflammatory, antiproliferative, cytoprotective, and apoptotic activities, whose mol. targets are unknown. Using both cell-free and cellular assays, we show that CDDO-Im is a direct inhibitor of IκB kinase (IKK)β and that it thereby inhibits binding of nuclear factor-κB to DNA and subsequent transcriptional activation. Pretreatment of cells with CDDO-Im prevents IκBα phosphorylation and degradation in response to tumor necrosis factor α. The kinetics of this inhibition by CDDO-Im are rapid and occur within 15 min. A biotinylated analog of CDDO-Im showed that CDDO-Im binds to the IKK signalsome. Furthermore, we show that Cys179 on IKK is a target for CDDO-Im. This is the first report to show that this novel synthetic triterpenoid binds to and inhibits IKKβ directly.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1220460 CAPLUS

DOCUMENT NUMBER: 146:134811

TITLE: Triterpenoid CDDO-Me blocks the NF-κB pathway by direct inhibition of IKKβ on cys-179

AUTHOR(S): Ahmad, Rehan; Raina, Deepak; Meyer, Colin; Kharbanda, Surender; Kufe, Donald

CORPORATE SOURCE: Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, 02115, USA

SOURCE: Journal of Biological Chemistry (2006), 281(47), 35764-35769
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The novel oleanane triterpenoid 2-cyano-3,12-dioxooleana-1,9,-dien-28-oic acid (CDDO) and the C-28 Me ester (CDDO-Me) induce apoptosis of human tumor cells by disruption of redox balance and are currently in clin. trials. The present studies show that CDDO and CDDO-Me block tumor necrosis factorα-induced targeting of NF-κB p65 to the nucleus. CDDO-Me also blocked tumor necrosis factor α-induced phosphorylation of IκBα. In concert with these results, we found that CDDO-Me inhibits IκBα

kinaseβ (IKKβ) activity in cells. In support of a direct mechanism, CDDO-Me inhibited recombinant IKKβ activity in vitro. The results also demonstrate that (i) CDDO and CDDO-Me form adducts with IKKβ, but not IKKβ with mutation of Cys-179 to Ala, and (ii) CDDO-Me inhibits IKKβ by a mechanism dependent on oxidation of Cys-179. These findings indicate that CDDO and CDDO-Me directly block IKKβ activity and thereby the NF-κB pathway by interacting with Cys-179 in the IKKβ activation loop.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:823024 CAPLUS

DOCUMENT NUMBER: 146:220301

TITLE: Depletion of intracellular glutathione contributes to JNK-mediated death receptor 5 upregulation and apoptosis induction by the novel synthetic triterpenoid methyl-2-cyano-3, 12-dioxooleana-1, 9-dien-28-oate (CDDO-Me)

AUTHOR(S): Yue, Ping; Zhou, Zhongmei; Khuri, Fadlo R.; Sun, Shi-Yong

CORPORATE SOURCE: Department of Hematology and Oncology; Winship Cancer Institute, Emory University of School of Medicine, Atlanta, GA, USA

SOURCE: Cancer Biology & Therapy (2006), 5(5), 492-497
CODEN: CBTAAO; ISSN: 1538-4047

PUBLISHER: Landes Bioscience

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The novel synthetic triterpenoid methyl-2-cyano-3, 12-dioxooleana-1, 9-dien-28-oate (CDDO-Me) induces apoptosis in human cancer cells, showing potential as a cancer therapeutic agent. We previously demonstrated that CDDO-Me induces a c-Jun N-terminal kinase (JNK)-mediated DR5 expression and apoptosis. This study revealed the mechanism by which CDDO-Me induces JNK activation and subsequent DR5 upregulation and apoptosis. To determine whether CDDO-Me activates JNK and induces DR5 expression and apoptosis via oxidative stress by inducing the generation of reactive oxygen species (ROS), we examined the effects of various antioxidants on JNK activation, DR5 upregulation, and apoptosis induction by CDDO-Me. Thiol antioxidants, including N-acetyl-L-cysteine (NAC), glutathione (GSH) and dithiothrietol (DTT), abrogated CDDO-Me-induced apoptosis. In contrast, nonthiol antioxidants, including butylated hydroxyanisole (BHA), Trolox, mannitol, and Mn(II) tetra(4-benzoic acid) porphyrin chloride (MnTBAP), failed to do so, with the exception of vitamin C (Vit C). Accordingly, only thiol antioxidants blocked JNK activation induced by CDDO-Me. CDDO-Me reduced intracellular levels of GSH; this reduction was abrogated only by thiol antioxidants and Vit C. However, CDDO-Me did not promote ROS generation. These results suggest that depletion of intracellular GSH, but not ROS generation, contributes to CDDO-Me-induced JNK activation and apoptosis, at least in our systems. Furthermore, these thiol antioxidants abrogated CDDO-Me-induced DR5 expression, whereas the GSH-depleting agent diethylmaleate also upregulated DR5 expression at concns. that deplete intracellular GSH, demonstrating that GSH depletion can cause DR5 upregulation. Collectively, we conclude that CDDO-Me activates the JNK pathway via depletion of intracellular GSH, leading to DR5 upregulation and induction of apoptosis.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:264028 CAPLUS

DOCUMENT NUMBER: 145:262581

TITLE: A Synthetic Triterpenoid, CDDO-Me, Inhibits IκBα Kinase and Enhances Apoptosis Induced

by TNF and Chemotherapeutic Agents through Down-Regulation of Expression of Nuclear Factor κB-Regulated Gene Products in Human Leukemic Cells

AUTHOR(S): Shishodia, Shishir; Sethi, Gautam; Konopleva, Marina; Andreeff, Michael; Aggarwal, Bharat B.

CORPORATE SOURCE: Cytokine Research Laboratory, Department of Experimental Therapeutics and Section of Molecular Hematology and Therapy, Department of Blood and Marrow Transplantation, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

SOURCE: Clinical Cancer Research (2006), 12(6), 1828-1838
CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The C-28 Me ester of 2-cyano-3,12-dioxoolean-1,9-dien-28-oic acid (CDDO-Me), a synthetic triterpenoid based on naturally occurring ursolic and oleanolic acids, induces apoptosis in tumor cells, induces differentiation, and inhibits inflammatory response through a poorly understood mechanism. Because the nuclear transcription factor nuclear factor κB (NF-κB) has been shown to suppress apoptosis and promote proliferation and is linked with inflammation and differentiation, we postulated that CDDO-Me modulates NF-κB activity and NF-κB-regulated gene expression. Using human leukemia cell lines and patient samples, we show that CDDO-Me potently inhibits both constitutive and inducible NF-κB activated by tumor necrosis factor (TNF), interleukin (IL)-1{szligbeta}, phorbol ester, okadaic acid, hydrogen peroxide, lipopolysaccharide, and cigarette smoke. CDDO-Me was more potent than CDDO and its imidazole derivative NF-κB suppression occurred through inhibition of IκBα kinase activation, IκBα phosphorylation, IκBα degradation, p65 phosphorylation, p65 nuclear translocation, and NF-κB-mediated reporter gene transcription. This inhibition correlated with suppression of NF-κB-dependent genes involved in antiapoptosis (IAP2, cFLIP, TRAF1, survivin, and bcl-2), proliferation (cyclin dl and c-myc), and angiogenesis (VEGF, cox-2, and mmp-9). CDDO-Me also potentiated the cytotoxic effects of TNF and chemotherapeutic agents. Overall, our results suggest that CDDO-Me inhibits NF-κB through inhibition of IκBα kinase, leading to the suppression of expression of NF-κB-regulated gene products and enhancement of apoptosis induced by TNF and chemotherapeutic agents.

REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:580980 CAPLUS

DOCUMENT NUMBER: 143:221979

TITLE: 2-Cyano-3,12-dioxoolean-1,9-dien-28-oic acid and related compounds inhibit growth of colon cancer cells through peroxisome proliferator-activated receptor γ-dependent and -independent pathways

AUTHOR(S): Chintharlapalli, Sudhakar; Papineni, Sabitha; Konopleva, Marina; Andreef, Michael; Samudio, Ismael; Safe, Stephen

CORPORATE SOURCE: Department of Biochemistry and Biophysics, Texas A and M University, College Station, TX, USA

SOURCE: Molecular Pharmacology (2005), 68(1), 119-128
CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 2-Cyano-3,12-dioxoolean-1,9-dien-28-oic acid (CDDO) and the corresponding

Me (CDDO-Me) and imidazole (CDDO-Im) esters induce peroxisome proliferator-activated receptor γ (PPARγ)-dependent transactivation in SW-480 colon cancer cells, and these responses were inhibited by small inhibitory RNA for PPARγ. Moreover, in a mammalian two-hybrid assay using the PPARγ2-VP16 fusion plasmid and GAL4-coactivator/corepressor chimeras and a construct (pGAL4) containing five tandem GAL4 response elements, CDDO, CDDO-Me, and CDDO-IM induce transactivation and PPARγ interaction with multiple coactivators. A major difference among the three PPARγ agonists was the higher activity of CDDO-Im to induce PPARγ interactions with the corepressor SMRT. CDDO, CDDO-Me, and CDDO-Im inhibited SW-480, HCT-116, and HT-29 colon cancer cell proliferation at low concns. and induced cell death at higher concns. Growth inhibition at lower concns. correlated with induction of the tumor suppressor gene caveolin-1 which is known to inhibit colon cancer cell growth. Induction of caveolin-1 by CDDO, CDDO-Me, and CDDO-Im was inhibited by the PPARγ antagonist N-4'-aminopyridyl-2-chloro-5-nitrobenzamide (T007), whereas higher doses induced apoptosis [poly(ADP-ribose) polymerase cleavage], which was not inhibited by T007. These results illustrate that CDDO-, CDDO-Me, and CDDO-Im induce both PPARγ-dependent and -independent responses in colon cancer cells, and activation of these pathways are separable and concentration-dependent for all three compds.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:480865 CAPLUS
DOCUMENT NUMBER: 143:166163
TITLE: Triterpenoid CDDO-Im downregulates PML/RARα expression in acute promyelocytic leukemia cells
AUTHOR(S): Ikeda, T.; Kimura, F.; Nakata, Y.; Sato, K.; Ogura, K.; Motoyoshi, K.; Sporn, M.; Kufe, D.
CORPORATE SOURCE: Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Cell Death and Differentiation (2005), 12(5), 523-531
CODEN: CDDIEK; ISSN: 1350-9047
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The triterpenoid 2-cyano-3,12-dioxooleana-1,9-dien-28-oic acid (CDDO) induces differentiation and apoptosis of diverse human tumor cells. In the present study, we examined the effects of the CDDO imidazolide imide (CDDO-Im) on the NB4 acute promyelocytic leukemia (APL) cell line and primary APL cells. The results show that CDDO-Im selectively downregulates expression of the PML/retinoic receptor alpha fusion protein by a caspase-dependent mechanism and sensitizes APL cells to the differentiating effects of all-trans retinoic acid (ATRA). CDDO-Im treatment of APL cells was also associated with disruption of redox balance and activation of the extrinsic apoptotic pathway. In concert with these results, CDDO-Im sensitizes APL cells to arsenic trioxide (ATO)-induced apoptosis. Our findings indicate that CDDO-Im may be effective in the treatment of APL by: (i) downregulation of PML/RARα; (ii) enhancement of ATRA-induced differentiation; and (iii) sensitization of ATO-induced APL cell death.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:670953 CAPLUS
DOCUMENT NUMBER: 141:342861
TITLE: Design, Synthesis, and Biological Evaluation of Biotin Conjugates of 2-Cyano-3,12-dioxooleana-1,9(11)-dien-28-oic Acid for the Isolation of the Protein Targets
AUTHOR(S): Honda, Tadashi; Janosik, Tomasz; Honda, Yukiko; Han, Jie; Liby, Karen T.; Williams, Charlotte R.; Couch,

Robin D.; Anderson, Amy C.; Sporn, Michael B.; Gribble, Gordon W.
CORPORATE SOURCE: Department of Chemistry, Dartmouth College, Hanover, NH, 03755, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(20), 4923-4932
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:342861
AB 2-Cyano-3,12-dioxooleana-1,9(11)-dien-28-oic acid (CDDO) and related compds. [for example, CDDO-Me and CDDO-Im] are potential anti-inflammatory, cancer chemopreventive, and chemotherapeutic agents. However, the mechanisms responsible for the multiple effects of CDDO are still unclear. Clarification of these mechanisms and particularly isolation of the protein targets are essential for the development of CDDO and its analogs as clin. useful drugs. Such knowledge would provide superior opportunities for designing new compds. with improved potency and selectivity. Therefore, to isolate protein targets using affinity chromatog. with immobilized streptavidin as a carrier, we have designed and synthesized C-17 and C-23 biotin conjugates of CDDO on the basis of our established structure-activity relationships. For the synthesis of one compound , a new important precursor, 23-hydroxy-CDDO-Me was synthesized from 20 by a C-23 oxidation protocol, which involves cyclopalladation of the C-4 Me group from a 3-one oxime. The inhibitory activity of C-23 conjugate is only about 3 times less potent than the mother compound, CDDO, against the proliferation of MCF-7 breast cancer cells. Consequently, it may be a very promising tool for the isolation of the protein targets of CDDO.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:832882 CAPLUS
DOCUMENT NUMBER: 140:399426
TITLE: Synthetic triterpenoids activate a pathway for apoptosis in AML cells involving downregulation of FLIP and sensitization to TRAIL
AUTHOR(S): Suh, W.-S.; Kim, Y. S.; Schimmer, A. D.; Kitada, S.; Minden, M.; Andreeff, M.; Suh, N.; Sporn, M.; Reed, J. C.
CORPORATE SOURCE: The Burnham Institute, La Jolla, CA, 92037, USA
SOURCE: Leukemia (2003), 17(11), 2122-2129
CODEN: LEUKED; ISSN: 0887-6924
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Acute myelogenous leukemia (AML) remains a deadly disease for most adult patients, due primarily to the emergence of chemoresistant cells. Defects in apoptosis pathways make important contributions to chemoresistance, suggesting a need to restore apoptosis sensitivity or to identify alternative pathways for apoptosis induction. Triterpenoids represent a class of naturally occurring and synthetic compds. with demonstrated antitumor activity, including 2-cyano-3,12-dioxoolean-1,9-dien-28-oic acid (CDDO) and its Me ester (CDDO-m). We explored the effects of CDDO and CDDO-m in vitro on established AML cell lines (HL-60, U937, AML-2) and on freshly isolated AML blasts. CDDO and CDDO-m reduced the viability of all AML cell lines tested in a dose-dependent manner, with EDs for killing 50% of cells (ED50) within 48 h of .apprx.1 and 0.5 μM, resp. CDDO or CDDO-m also induced substantial increases in cell death in five out of 10 samples of primary AML blasts. Cell death induced by CDDO and CDDO-m was attributed to apoptosis, based on characteristic cell morphol. and evidence of caspase activation. Immunoblot anal. demonstrated proteolytic processing of caspase-3, -7, and -8, but not caspase-9, suggesting the

involvement of the extrinsic' pathway, linked to apoptosis induction by TNF-family death receptors. Accordingly, CDDO and CDDO-m induced concentration-dependent redns. in the levels of FLIP protein, an endogenous antagonist of caspase-8, without altering the levels of several other apoptosis-relevant proteins. Redns. in FLIP were rapid, detectable within 3 h after exposure of AML cell lines to CDDO or CDDO-m. CDDO and CDDO-m also sensitized two of four leukemia lines to TRAIL, a TNF-family death ligand. The findings suggest that synthetic triterpenoids warrant further investigation in the treatment of AML, alone or in combination with TRAIL or other immune-based therapies.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:505732 CAPLUS
DOCUMENT NUMBER: 138:66283
TITLE: An inducible pathway for degradation of FLIP protein sensitizes tumor cells to TRAIL-induced apoptosis
AUTHOR(S): Kim, Youngsoo; Suh, Nanjoo; Sporn, Michael; Reed, John C.
CORPORATE SOURCE: Burnham Institute, La Jolla, CA, 92037, USA
SOURCE: Journal of Biological Chemistry (2002), 277(25), 22320-22329
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB TRAIL (Apo2 ligand) is a member of the tumor necrosis factor (TNF) family of cytokines that induces apoptosis. Because TRAIL preferentially kills tumor cells, sparing normal tissues, interest has emerged in applying this biol. factor for cancer therapy in humans. However, not all tumors respond to TRAIL, raising questions about resistance mechanisms. We demonstrate here that a variety of natural and synthetic ligands of peroxisome proliferator-activated receptor-γ (PPARγ) sensitize tumor but not normal cells to apoptosis induction by TRAIL. PPARγ ligands selectively reduce levels of FLIP, an apoptosis-suppressing protein that blocks early events in TRAIL/TNF family death receptor signaling. Both PPARγ agonists and antagonists displayed these effects, regardless of the levels of PPARγ expression and even in the presence of a PPARγ dominant-neg. mutant, indicating a PPARγ-independent mechanism. Redns. in FLIP and sensitization to TRAIL-induced apoptosis were also not correlated with NF-κB, further suggesting a novel mechanism. PPARγ modulators induced ubiquitination and proteasome-dependent degradation of FLIP, without concomitant redns. in FLIP mRNA. The findings suggest the existence of a pharmacol. regulated novel target of this class of drugs that controls FLIP protein turnover, and raise the possibility of combining PPARγ modulators with TRAIL for more efficacious elimination of tumor cells through apoptosis.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:465747 CAPLUS
DOCUMENT NUMBER: 137:41724
TITLE: CDDO (2-cyano-3,12-dioxoolean-1,9-dien-28-oic acid) compounds and combinations with other chemotherapeutics for the treatment of cancer and graft vs. host disease
INVENTOR(S): Konopleva, Marina; Andreeff, Michael; Sporn, Michael
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 184 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002047611	A2	20020620	WO 2001-US44541	20011128
WO 2002047611	A8	20030626		
WO 2002047611	A3	20031224		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2430454	A1	20020620	CA 2001-2430454	20011128
AU 2002043246	A5	20020624	AU 2002-43246	20011128
US 2003119732	A1	20030626	US 2001-998009	20011128
EP 1395255	A2	20040310	EP 2001-989130	20011128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			US 2000-253673P P	20001128
			WO 2001-US44541 W	20011128

AB CDDO compds. in combination with other chemotherapeutic agents induce and potentiate cytotoxicity and apoptosis in cancer cells. One class of chemotherapeutic agents include retinoids. Cancer therapies based on these combination therapies are provided. Also provided are methods to treat graft vs. host diseases using the CDDO compds.

L5 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:95270 CAPLUS
DOCUMENT NUMBER: 136:379616
TITLE: Identification of a novel synthetic triterpenoid, methyl-2-cyano-3,12-dioxooleana-1,9-dien-28-oate, that potently induces caspase-mediated apoptosis in human lung cancer cells
AUTHOR(S): Kim, Kevin B.; Lotan, Reuben; Yue, Ping; Sporn, Michael B.; Suh, Nanjoo; Gribble, Gordon W.; Honda, Tadashi; Wu, Gen Sheng; Hong, Waun Ki; Sun, Shi-Yong
CORPORATE SOURCE: Department of Thoracic/Head and Neck Medical Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Molecular Cancer Therapeutics (2002), 1(3), 177-184
CODEN: MCTOCF; ISSN: 1535-7163
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lung cancer continues to be the leading cause of cancer -related death in the United States. Therefore, new agents targeting prevention and treatment of lung cancer are urgently needed. In the present study, we demonstrate that a novel synthetic triterpenoid methyl-2-cyano-3,12-dioxooleana-1,9-dien-28-oate (CDDO-Me) is a potent inducer of apoptosis in human non-small cell lung carcinoma (NSCLC) cells. The concns. required for a 50% decrease in cell survival (IC50) ranged from 0.1 to 0.3 μM. CDDO-Me induced rapid apoptosis and triggered a series of effects associated with apoptosis including a rapid release of cytochrome c from mitochondria, activation of procaspase-9, -7, -6, and -3, and cleavage of poly(ADP-ribose) polymerase and lamin A/C. Moreover, the caspase-3 inhibitor Z-DEVD-FMK and the pan caspase inhibitor Z-VAD-FMK

suppressed CDDO-Me-induced apoptosis. These results indicate that CDDO-Me induced apoptosis in human NSCLC cells via a cytochrome c-triggered caspase activation pathway. CDDO-Me did not alter the level of Bcl-2 and Bcl-xL proteins, and no correlation was found between cell sensitivity to CDDO-Me and basal Bcl-2 expression level. Furthermore, overexpression of Bcl-2 did not protect cells from CDDO-Me-induced apoptosis. These results suggest that CDDO-Me induces apoptosis in NSCLC cells irresp. of Bcl-2 expression level. In addition, no correlation was found between cell sensitivity to CDDO-Me and p53 status, suggesting that CDDO-Me induce a p53-independent apoptosis. Our results demonstrate that CDDO-Me may be a good candidate for addnl. evaluation as a potential therapeutic agent for human lung cancers and possibly other types of cancer.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:632697 CAPLUS

DOCUMENT NUMBER: 133:350364

TITLE: Synthetic Oleanane and Ursane Triterpenoids with Modified Rings A and C: A Series of Highly Active Inhibitors of Nitric Oxide Production in Mouse Macrophages

AUTHOR(S): Honda, Tadashi; Rounds, BarbieAnn V.; Bore, Lothar; Finlay, Heather J.; Favaloro, Frank G. ,Jr.; Suh, Nanjoo; Wang, Yongping; Sporn, Michael B.; Gribble, Gordon W.

CORPORATE SOURCE: Department of Chemistry, Dartmouth College Dartmouth Medical School, Hanover, NH, 03755, USA

SOURCE: Journal of Medicinal Chemistry (2000), 43(22), 4233-4246
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 133:350364

AB New olean- and urs-1-en-3-one triterpenoids with various modified rings C have been synthesized as potential antiinflammatory and cancer chemopreventive agents and evaluated for their inhibitory activities against production of nitric oxide induced by interferon-γ in mouse macrophages. These studies revealed that 9(11)-en-12-one and 12-en-11-one functionalities in ring C increase the potency by about 2-10 times compared with the original 12-ene. Subsequently, novel olean- and urs-1-en-3-one derivs. with nitrile and carboxyl groups at C-2 in ring A and with 9(11)-en-12-one and 12-en-11-one functionalities in ring C were synthesized. Among them, Me 2-cyano-3, 12-dioxooleana-1,9(11)-dien-28-oate, 2-cyano-3,12-dioxooleana-1,9(11)-dien-28-oic acid (CDDO) (I), and Me 2-carboxy-3,12-dioxooleana-1,9(11)-dien-28-oate were found to have extremely high potency (IC50 = 0.1 nM level). Their potency is similar to that of dexamethasone although they do not act through the glucocorticoid receptor. Overall, the combination of modified rings A and C increases the potency by about 10 000 times compared with the lead compound, 3-oxooleana-1,12-dien-28-oic acid (IC50 = 1 μM level). The selected oleanane triterpenoid, I, was found to be a potent, multifunctional agent in various in vitro assays and to show antiinflammatory activity against thioglycollate-interferon-γ-induced mouse peritonitis.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:811070 CAPLUS

DOCUMENT NUMBER: 132:44971

TITLE: Therapeutic triterpenoid compositions and methods of use for treatment of cancer, neurodegenerative, diseases, and inflammatory bowel diseases

INVENTOR(S): Gribble, Gordon W.; Honda, Tadashi; Sporn, Michael B.; Suh, Nanjoo
PATENT ASSIGNEE(S): Trustees of Dartmouth College, USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9965478	A1	19991223	WO 1999-US13635	19990618
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6326507	B1	20011204	US 1999-335003	19990617
CA 2335505	A1	19991223	CA 1999-2335505	19990618
EP 1089724	A1	20010411	EP 1999-928731	19990618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002530272	T	20020917	JP 2000-554358	19990618
US 2002042535	A1	20020411	US 2001-927081	20010809
US 6552075	B2	20030422		
US 2003236303	A1	20031225	US 2003-395372	20030324
US 7288568	B2	20071030		
US 2005288363	A1	20051229	US 2005-121316	20050503

PRIORITY APPLN. INFO.:

US 1998-90053P	P	19980619
US 1999-335003	A	19990617
WO 1999-US13635	W	19990618
US 2001-927081	A1	20010809
US 2003-395372	A1	20030324

OTHER SOURCE(S): MARPAT 132:44971
AB Triterpenoid compds., e.g. 2-cyano-3,12-dioxoolean-1,9-dien--28-oic acid, and methods are disclosed which are useful for chemopreventative treatment of diseases such as cancer, Alzheimer's disease, Parkinson's disease, inflammatory bowel diseases, and multiple sclerosis.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2005:331377 USPATFULL
TITLE: Therapeutic compositions and methods of use
INVENTOR(S): Gribble, Gordon W., Norwich, VT, UNITED STATES
Honda, Tadashi, Hanover, NH, UNITED STATES
Sporn, Michael B., Tunbridge, VT, UNITED STATES
Suh, Nanjoo, Hanover, NH, UNITED STATES
PATENT ASSIGNEE(S): Trustees of Dartmouth College (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005288363	A1	20051229
APPLICATION INFO.:	US 2005-121316	A1	20050503 (11)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2003-395372, filed on 24 Mar 2003, PENDING
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FULBRIGHT & JAWORSKI L.L.P., 600 CONGRESS AVE., SUITE 2400, AUSTIN, TX, 78701, US
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Page(s)
LINE COUNT: 931
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds and methods useful for chemopreventative treatment of diseases

such as cancer, Alzheimer's disease, Parkinson's disease, inflammatory bowel diseases, and multiple sclerosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 17 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2003:335425 USPATFULL
TITLE: Therapeutic compositions and methods of use
INVENTOR(S): Gribble, Gordon W., Norwich, VT, UNITED STATES
Honda, Tadashi, Hanover, NH, UNITED STATES
Sporn, Michael B., Tunbridge, VT, UNITED STATES
Suh, Nanjoo, Hanover, NH, UNITED STATES
PATENT ASSIGNEE(S): Trustees of Darmouth College (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003236303	A1	20031225
	US 7288568	B2	20071030
APPLICATION INFO.:	US 2003-395372	A1	20030324 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-927081, filed on 9 Aug 2001, GRANTED, Pat. No. US 6552075 Division of Ser. No. US 1999-335003, filed on 17 Jun 1999, GRANTED, Pat. No. US 6326507

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-90053P	19980619 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Steven L. Highlander, Esq., FULBRIGHT & JAWORSKI L.L.P., Suite 2400, 600 Congress Avenue, Austin, TX, 78701
NUMBER OF CLAIMS: 73
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 14 Drawing Page(s)
LINE COUNT: 1146
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds and methods useful for chemopreventative treatment of diseases such as cancer, Alzheimer's disease, Parkinson's disease, inflammatory bowel diseases, and multiple sclerosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INSTANT APP.

L5 ANSWER 18 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2003:173884 USPATFULL
TITLE: CDDO-compounds and combination therapies thereof
INVENTOR(S): Konopleva, Marina, Houston, TX, UNITED STATES
Andreeff, Michael, Houston, TX, UNITED STATES
Sporn, Michael B., Tunbridge, VT, UNITED STATES
PATENT ASSIGNEE(S): Board of (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003119732	A1	20030626
APPLICATION INFO.:	US 2001-998009	A1	20011128 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-253673P	20001128 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Priya D. Subramony, Fulbright & Jaworski L.L.P., 600 Congress Avenue, Suite 2400, Austin, TX, 78701
NUMBER OF CLAIMS: 79
EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 35 Drawing Page(s)
LINE COUNT: 5276
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB CDDO-compounds in combination with other chemotherapeutic agents induce and potentiate cytotoxicity and apoptosis in cancer cell. One class of chemotherapeutic agents include retinoids. Cancer therapies based on these combination therapies are provided. Also provided are methods to treat graft versus host diseases using the CDDO compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 19 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2002:78876 USPATFULL
TITLE: Therapeutic compounds and methods of use
INVENTOR(S): Gribble, Gordon W., Norwich, VT, UNITED STATES
Honda, Tadashi, Hanover, NH, UNITED STATES
Sporn, Michael B., Tunbridge, VT, UNITED STATES
Suh, Nanjoo, Hanover, NH, UNITED STATES
PATENT ASSIGNEE(S): Trustees of Dartmouth College (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20020042535	A1	20020411
	US 6552075	B2	20030422
APPLICATION INFO.:	US 2001-927081	A1	20010809 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1999-335003, filed on 17 Jun 1999, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-90053P	19980619 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Steven L. Highlander, FULBRIGHT & JAWORSKI L.L.P., Suite 2400, 600 Congress Avenue, Austin, TX, 78701
NUMBER OF CLAIMS: 73
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Page(s)
LINE COUNT: 1150
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds and methods useful for chemopreventative treatment of diseases such as cancer, Alzheimer's disease, Parkinson's disease, inflammatory bowel diseases, and multiple sclerosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 20 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2001:221178 USPATFULL
TITLE: Therapeutic compounds and methods of use
INVENTOR(S): Gribble, Gordon W., Norwich, VT, United States
Honda, Tadashi, Hanover, NH, United States
Sporn, Michael B., Tunbridge, VT, United States
Suh, Nanjoo, Hanover, NH, United States
PATENT ASSIGNEE(S): Trustees of Dartmouth College, Hanover, NH, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6326507	B1	20011204
APPLICATION INFO.:	US 1999-335003		19990617 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-90053P	19980619 (60)

```
DOCUMENT TYPE:          Utility
FILE SEGMENT:           GRANTED
PRIMARY EXAMINER:       Higel, Floyd D.
ASSISTANT EXAMINER:     Sackey, Ebenezer
LEGAL REPRESENTATIVE:   Fulbright & Jaworski, LLP
NUMBER OF CLAIMS:       13
EXEMPLARY CLAIM:        1
NUMBER OF DRAWINGS:     14 Drawing Figure(s); 11 Drawing Page(s)
LINE COUNT:             964
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB      Compounds and methods useful for chemopreventative treatment of diseases
        such as cancer, Alzheimer's disease, Parkinson's disease,
        inflammatory bowel diseases, and multiple sclerosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.


=> d his

     (FILE 'HOME' ENTERED AT 11:41:16 ON 07 NOV 2007)

     FILE 'REGISTRY' ENTERED AT 11:41:28 ON 07 NOV 2007
L1              STRUCTURE UPLOADED
L2            0 S L1
L3            2 S L1 FULL

     FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 11:42:29 ON 07 NOV
     2007
L4           30 S L3
L5           20 S L4 AND (CANCER OR TUMOR)

=>

---Logging off of STN---


=>
Executing the logoff script...


=> LOG Y

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      63.44     238.15

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                     -11.70     -11.70

STN INTERNATIONAL LOGOFF AT 11:43:14 ON 07 NOV 2007
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